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UNITED STATES DISTRICT COURT

NORTHERN DISTRICT OF CALIFORNIA

SAN JOSE DIVISION

HOLOGIC, INC., CYTYC CORPORATION, and HOLOGIC L.P.,

Plaintiffs,

vs.

SENORX, INC.,

Defendant.

AND RELATED COUNTERCLAIMS.

Case No. C08 00133 RMW (RS)

PLAINTIFFS' REPLY BRIEF IN SUPPORT OF MOTION FOR PRELIMINARY INJUNCTION

Date: April 21, 2008
Time: 2:00 p.m.
Courtroom: 6, 4th Floor
Judge: Hon. Ronald M. Whyte

TABLE OF CONTENTS

TABLE OF AUTHORITIES

Page(s)

CASES

SenoRx's Opposition reveals that it has little response to Hologic's claims of patent infringement, particularly with regard to the '204 patent. And the documents produced and depositions taken within the last week establish that SenoRx has: (1) REDACTED [redacted] (2) marketed its Contura product as superior to Hologic's Mammosite despite the absence of a clinical study (or even peer-reviewed article) establishing Contura's effectiveness, let alone superiority; and (3) based its superiority claims on a treatment protocol that conflicts with its FDA clearance and that may present significant patient risk. A preliminary injunction is particularly appropriate under the circumstances of this case.

I. HOLOGIC WILL SUCCEED ON THE MERITS OF INFRINGEMENT CLAIMS

SenoRx has claimed with reference to Hologic's MammoSite product (which is a commercial embodiment of the '204 patent) that the Contura was designed to have the REDACTED [redacted] Ex. O[1] at 6606. It should be no surprise, then, that the Contura practices claims of the same patents embodied by the MammoSite.

A. Claim 36 Of The '204 Patent Is Valid And Infringed

SenoRx's assertion of noninfringement, which is based on a single, purportedly un-met claim limitation, borders on the frivolous. And its claim of invalidity, which relies upon a single reference, cited during prosecution to the examiner is no stronger.

1. The Contura Infringes Claim 36 Of The '204 Patent

SenoRx apparently concedes that the Contura infringes each limitation of claim 36 of the '204 patent except for the requirement that the radiation source be "disposed in the inner spatial volume." The Court previously construed this limitation in the *Xoft* case:

> a region of space surrounded by an outer spatial volume and either enclosed by a polymeric film wall or defined by the outside surface of a solid radionuclide sphere.

[1] Unless otherwise noted, cited exhibits refer to exhibits attached to the Declaration of Katharine L. Altemus In Support of Plaintiffs' Reply Brief In Support of Motion For Preliminary Injunction ("Altemus Decl.").

Ex. OO. As demonstrated by Hologic in its Motion, and undisputed by SenoRx, the Contura's radionuclide is within a cylindrical, polymeric wall (a lumen) during treatment which is in turn surrounded by a balloon.[2] The Contura thus facially satisfies every element of Claim 36.

Unable to deny that the literal language of the Court's claim construction reads on the Contura, SenoRx suggests that Hologic is departing from the *spirit* of that language in two ways. Opp. at 6. *First*, SenoRx contends that the '204 patent "makes clear that lumens ['labeled as numbers 14 and 16'] and the 'inner spatial volume' are different things." *Id*. SenoRx cannot, of course, point to any express language suggesting that the inner spatial volume cannot be a lumen or other cylindrical shape. Rather, the argument is that, because there is a reference to certain lumens in the same passage of the specification that also discusses the inner spatial volume, then lumens and the inner spatial volume must be different.

The obvious flaw with this argument is that the referenced lumens 14 and 16 are expressly described as inflation lumens, *i.e.*, they are the tubes through which air or fluid are pumped to inflate the balloons. The radionuclide of the '204 patent is ***not*** contained within lumens 14 and 16 during treatment, and thus it is hardly surprising that the specification distinguishes between these lumens and the inner spatial volume. This is precisely the same structure as the Contura, which has one set of lumens for inflation and a different polymeric structure for enclosing the radionuclide.[3] Far from a "dissociation" of the Court's construction from its reasoning as SenoRx contends (*Id*.), the Contura lumen serves precisely the role that the Court suggested in its construction, *i.e.*, providing a physical boundary between the radionuclide and the fluid (be it air or liquid) contained within the outer spatial volume.

Second, SenoRx contends that the lumens in the Contura are not "surrounded by" the outer spatial volume because the lumens extend into the catheter shaft. Initially, this is a misreading of the Court's construction as it is a particular "region of space" composed of a polymer-enclosed

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[2] Absent the polymer, the radionuclide itself could define the inner spatial volume as construed.

[3] If SenoRx is suggesting that the polymeric wall must be spherical – as opposed to, *e.g.*, the cylindrical shape of the Contura – such a position is expressly at odds with the specification. *See, e.g.,* Ex. ___ at 5:13-16 ['204 patent] "it is not essential to the invention that the volumes 30 [the inner spatial volume] . . . have spherical walls. . . ."

radionuclide that must be surrounded. There is no dispute that, during treatment, Contura's radionuclide is surrounded by the outer balloon. And the fact that the lumens in the Contura are in fluid communication with the shaft of the catheter cannot mean that the polymeric-enclosed radionuclide is not "surrounded by" the balloon because to so hold would be to exclude the preferred embodiment from the claims. See, e.g., Ex. P at 3:57-65, Figs. 1 and 5.

This conclusion is underscored by SenoRx's description of its products outside the context of this litigation. For example, in its Product Overview, SenoRx states that the device "allows for placement of a radiation source at the center or close to the center of the balloon. . . ." Ex. Q at SRX-HOL00004120; *See also* Ex. R at SRX-HOL00006488 (describing lumens as "1 central, 4 offset (5mm) from center"; *Id.* at SRX-HOL00006492 ("Central lumen/central dwell"). To argue that something that is positioned at the center of the balloon is not also surrounded by the balloon is absurd.

2. Claim 36 Of The '204 Patent Is Valid

The one piece of prior art cited by SenoRx against the '204 patent – an article by Ashpole, *et al.* – is hardly new: Hologic cited that art to the examiner during prosecution, and the examiner considered it prior to allowance and issuance of the claims. Ex. S at 316. Prior art considered by the examiner during prosecution is unlikely to create a substantial question of invalidity. *Glaxo Group Ltd. v. Apotex, Inc.,* 376 F.3d 1339, 1348 (Fed.Cir.2004). Further, Xoft's decision to take a license to the '204 patent is probative evidence of its validity. *Cf. WMS Gaming, Inc. v. Int'l Game Tech.*, 184 F.3d 1339, 1359 (Fed. Cir. 1999) ("Objective evidence of nonobviousness may include . . . licenses showing industry respect.").

In any event, Ashpole cannot invalidate the '204 patent because it fails to disclose, expressly or inherently, the final, critical limitation of claim 36 of the '204 patent:

> ***wherein the inner and outer spatial volumes are configured to provide a minimum prescribed absorbed dose for delivering therapeutic effects to a target tissue***, the target tissue being defined between the outer spatial volume expandable surface and a minimum distance outward from the outer spatial volume expandable surface, ***the apparatus providing a controlled dose at the outer spatial volume expandable surface to reduce or prevent necrosis in healthy tissue proximate to the expandable surface.***

(Emphases added.) For example, Ashpole does not disclose "providing a controlled dose at the outer spatial volume expandable surface to reduce or prevent necrosis in healthy tissue proximate to the

expandable surface." Verhey Decl. [4] ¶ 15. Ashpole notes that "[t]he dose at the surface of the balloon . . . can be as high as 70 Gy," notwithstanding the fact that "the limited tolerance of normal brain has restricted the maximum permissible dose to about 55-60 Gy." Ex. T at 333, 336; Verhey Decl. ¶ 18. Because 70 Gray is acknowledged to be above the maximum permissible dose for the brain, Ashpole expressly discloses a device that does not reduce or avoid necrosis of healthy tissue proximate to the expandable surface of the balloon. *Id.* As Dr. Orton testified:

> **Q**. [I]f a physician told that you 70 Gy was a lethal dose, and I would ask you to accept that for purposes of this question, you would agree that Ashpole does not disclose controlling the dose at the surface of the balloon so that it is not so high that it lethally damages healthy brain cells; right? [Objection omitted]
> **A** I don't think I could answer that, as a physicist, looking, reading this, it's – it's maybe what he [Ashpole] had in mind. I have no way of knowing.

Ex. U (Orton) at 33:10-20.[5]

While Ashpole mentions preventing radionecrosis in brain tissue, it purportedly solves this problem by providing a removable balloon applicator. Ex. T at 33, 36; Verhey Decl. ¶19. It does not teach anywhere the technique of Claim 36 of controlling the ratio of the dose at the expandable surface of the outer spatial volume to the prescribed dose at the depth of interest in the target issue so that the dose at the expandable surface is not so high that it lethally damages cells in healthy tissue in contact therewith. Verhey Decl. ¶ 17. Simply put, Ashpole discloses a fundamentally different approach than the '204 patent.

As another example, Ashpole does not disclose the provision of a "controlled dose," as required in the claim, because Ashpole does not describe inflating the balloon to press against the cavity walls and thereby conform the surgical margins to the shape of the balloon. Verhey Decl. ¶ 15. Without this conformity, a controlled dose cannot be administered because the shape of the resection cavity to be

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[4] Declaration of Lynn J. Verhey, Ph.D. In Support Of Plaintiffs' Motion For Preliminary Injunction ("Verhey Decl.").

[5] Ashpole also describes a "typical case [of] a balloon diameter of 2.9 cm" that provides a depth dose of 50 Gy at 0.5 cm from the surface of the balloon. Ex. T at 334; Verhey Decl. ¶ 18. Following the inverse square law, which Ashpole describes in his article as being operative, that would yield a dose of approximately 90 Gy at the surface of the balloon, assuming a symmetric distribution of sources within the balloon. *Id.*; Ex. U (Orton) at 63:11-15. Further, Ashpole's teaching of a minimum balloon diameter of 2.5 cm suggests that, for a dose of 50 Gy at 0.5 cm from the cavity, the dose at the surface can be even higher than 90 Gy. This is well over the "maximum permissible dose of about 55-60 Gy." *Id.*; Ex. T at 336.

treated must be radiographically ascertained. The fact that the Ashpole device is implanted into the brain teaches away from conforming the tissue to the balloon because the brain is particularly sensitive to compression and deformation. Verhey Decl. ¶¶ 14-15; Keisch Decl.[6] ¶ 14; Ex. MM (Cahill) at 128:4-9 ("And it is also my understanding, I think it says so in the response that we were discussing earlier, that generally when dealing with cavities of the brain, the balloon is chosen and inflated in a way so that it doesn't contact the tissue all the way around or push on the tissue."). The balloon on the Ashpole device, unlike the patented '204 invention, is used to fill as much of the resection cavity as possible, but is not used to conform the cavity to the three-dimensional shape of the balloon. Verhey Decl. ¶ 16. The Ashpole device simply cannot deliver a "controlled dose" to the tissue because the points on the balloon are not equidistant from the tissue in the tumor bed.

B. Claim 1 Of The '142 Patent Is Valid And Infringed

1. The Contura Infringes Claim 1 Of The '142 Patent

SenoRx's claim of non-infringement of Claim 1 the '142 patent is based on two claim construction arguments; there is no dispute that Contura infringes if Hologic's construction is accepted. *First*, SenoRx invites this Court to rewrite claim 1 to require "a radiation source [irreplaceably] disposed completely within the expandable outer surface." Ex. V at 9:1-2. While Hologic agrees that the phrases "replaceably disposable within" and "completely disposed within" do not have the same meaning, (Opp. at 16-17), the two phrases relate to entirely different—and independent—concepts. The phrase "replaceably disposable within" pertains whether the source can be replaced, whereas the phrase "completely disposed within" relates to how much of the radiation source is placed entirely within the outer balloon. Thus, in theory, a radiation source can simultaneously be "completely disposed within" the expandable outer surface and be "replaceably disposable within" the expandable outer surface.

Nothing in the specification or the prosecution history compels a different conclusion. The passage (Ex. V at 5:5-11) on which SenoRx relies in its brief completely fails to distinguish these

[6] Declaration of Martin E. Keisch, M.D. In Support Of Plaintiffs' Motion For Preliminary Injunction ("Keisch Decl.").

distinct concepts. Opp. at 17. Further, nothing in the prosecution history so much as hints that the amendment of claim 1 was a "clear and unmistakable surrender" of radiation sources that were replaceably disposable within the expandable outer surface. *See, e.g.*, *Vanguard Prods. Corp. v. Parker Hannifin Corp.*, 234 F.3d 1370, 1372 (Fed. Cir. 2000) ("[T]he prosecution history does not support [defendant's] argument that the … inventors "expressly disclaimed" claim scope

Second, SenoRx asserts that the term "apparatus volume" means the geometric volume of space defined by the expandable outer surface. Such a construction is at odds with how the inventor's characterized the term, and it would exclude all embodiments of their invention. See *Vitronics Corp. v. Conceptronic, Inc.*, 90 F.3d 1576, 1583 (Fed. Cir. 1996) (noting that a construction excluding all embodiments is "rarely, if ever correct and would require highly persuasive evidentiary support.") Indeed, the proper construction of the phrase "a radiation source . . . spaced apart from the apparatus volume" is one in which the claim term is not read in isolation, "but in the context of the entire patent, including the specification." *Phillips v. AWH Corp.*, 415 F.3d 1303, 1313 (Fed. Cir. 2005)(en banc).

In the specification and during prosecution, the inventors made clear that "spaced apart" referred to the positional relationship between the radiation source and the wall of the expandable outer surface element, and hence the target tissue. For example, the specification states that an "outer spatial volume 30" is "affixed to the tubular body 12." Ex. V at 4:27-30. This outer spatial volume is "defined by an outer polymeric film barrier 32 that is appropriately *spaced from the radioactive source*." *Id.* at 4:27-30. Indeed, the inventors distinguished the prior art on the basis that

> [T]he radiation source is disposed completely within the expandable surface and spaced apart from the apparatus volume. (See Page 8, line 23 to page 9 line 13, noting the advantages of providing the radiation source within the interstitial volume and spaced apart from the target tissue . . .).

Ex. PP at SRX-HOL0000216-217.

The inventors further stated that "the radiation source is arranged within the device so that asymmetric dosing appears *at the apparatus volume*," indicating that the apparatus volume is located adjacent to the band of tissue to be treated, and is not intended to be a geometric volume of space

encapsulated by the expandable outer surface. *Id.* at 7; *See also Id.* at 8 (comparing the balloon disclosed in the Apple reference to the "apparatus volume" of claim 1).[7] Thus, SenoRx has failed to present the "highly persuasive evidentiary support" necessary to exclude of all embodiments disclosed in the '142 patent. *Vitronics*, 90 F.3d at 1583. And, SenoRx's rhetoric notwithstanding, the Contura product (as Hologic has already shown) includes a radiation source "located so as to be spaced apart from the apparatus volume."[8]

2. Claim 1 Of The '142 Patent Is Valid

Attempting to manufacture a substantial question of validity, SenoRx ignores the language of the claims and tries to create disclosure where there is none. Specifically, SenoRx contends that the '774 patent, *sub silentio*, discloses a "radiation source . . . asymmetrically located and arranged within the expandable surface to provide predetermined asymmetric isodose curves with respect to the apparatus volume." Ex. V at 9:3-6. In fact, the '774 patent fails to mention either: (1) locating and arranging a radiation source "to provide predetermine asymmetric isodose curves;" or (2) the asymmetrical placement of a radiation source.

Initially, the '774 patent simply does not disclose a radiation source "located and arranged . . . to provide predetermined asymmetric isodose curves," as required by claim 1. Ex. V at 9:4-6 (claim 1);

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[7] SenoRx discusses at length the construction of the term "inner spatial volume" from the *Xoft* case. Although the '142 patent is a continuation-in-part of the '813 patent at issue in *Xoft*, the terms "apparatus volume" and "inner spatial volume" are different. Because (1) the claim terms are different and (2) the relevant specification and prosecution history are distinct with respect to the term "apparatus volume" and "spaced apart from the apparatus volume," SenoRx places far too much reliance on the construction of the '813 patent. *See, e.g.*, *Medtronic, Inc. v. Advanced Cardiovascular Systems, Inc.*, 248 F.3d 1303, 1315 (Fed. Cir. 2001) (refusing to use intrinsic evidence from parent application pertaining to a claim term different than the term under consideration); *cf. Elkay Mfg. Co. v. Ebco Mfg. Co.*, 192 F.3d 973, 980 (Fed. Cir. 1999) (citing *Jonsson v. The Stanley Works,* 903 F.2d 812, 817-818, (Fed.Cir.1990) for the proposition that "[w]hen multiple patents derive from the same initial application, the prosecution history regarding a claim limitation in any patent that has issued applies with equal force to subsequently issued patents *that contain the same claim limitation*" (emphasis added)).

[8] SenoRx does not claim that, if Hologic's construction is accepted, then the Claim is inoperable. In any event, inoperability of a claimed invention requires "a limitation that is *impossible* to meet." *Process Control Corp. v. HydReclaim Corp.*, 190 F.3d 1350, 1358-59 (Fed. Cir. 1999) (emphasis added). The claimed '142 invention can—and does— include a radiation source that is both within (i.e., surrounded by) an expandable outer surface and spaced apart from the apparatus volume (and the adjacent target tissue), as shown by the various embodiments detailed within the specification. The cases upon which SenoRx relies, in which "the *only possible interpretation* of the claim led to a nonsensical result," are inapposite. *Ortho-McNeil Pharm., Inc. v. Mylan Labs., Inc.*, 2008 WL 834402, *3 (Fed. Cir. Mar. 31, 2008) (emphasis added). "[C]laim 1 *can and should be interpreted as the patentees intended*", and as described in the specification and prosecution history. *Id*

Verhey Decl. ¶ 24. Dr. Orton—SenoRx's declarant—does not even attempt to supply the missing limitation; he only opines that a radiation oncologist or physicist "would have calculated the dose (and isodose profile)" prior to treatment. Orton Decl.[9] ¶ 50. Even if true, this is far from "locat[ing] and arrang[ing]" the radiation source "to provide *predetermined* isodose curves," as recited in claim 1 of the '142 patent. Ex. U (Orton) at 69:12-21. *Cf.* Verhey Decl. ¶ 24. Dr. Orton concurs, recognizing that where the inner balloon is fixed inside the outer balloon, he could not deliver prescribed isodose curves, if those prescribed curves were differently shaped. Ex. U (Orton) at 69:12-21[10].

Additionally, the '774 patent fails to disclose a radiation source "asymmetrically located and arranged within the expandable surface." Ex. V at 9:4-5. Apparently realizing this flaw, SenoRx contends that Figure 3 fills this gap. SenoRx is again mistaken. Under Federal Circuit precedent "it is well established that patent drawings do not define the precise proportions of the elements and may not be relied on to show particular sizes if the specification is completely silent on the issue." *Nystrom v. TREX Co., Inc.*, 424 F.3d 1136, 1149 (Fed. Cir. 2005). Not only is the '774 patent silent on any asymmetry in the placement of the radiation source, it states that Figure 3 is only a "schematic." Ex. UU at 3:1-2. Dr. Orton again concurs.[11] Ex. U (Orton) at 63:18-64:4. Therefore, this drawing cannot be used to determine the amount that the inner balloon is off-center, if it even is supposed to be off-center. Verhey Decl. ¶ 23.

The absence of these teachings in the '774 patent is fatal to SenoRx's invalidity arguments. Thus, SenoRx's defenses lack substantial merit and the '142 patent will withstand SenoRx's hand-waiving invalidity challenge.

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[9] Declaration of Colin G. Orton, Ph.D. In Support of Defendant's Opposition ("Orton Decl.").

[10] REDACTED [redacted]

II. THE EQUITABLE FACTORS MILITATE IN FAVOR OF INJUNCTIVE RELIEF

The equitable arguments proffered by SenoRx in opposition to Hologic's motion are largely, if not wholly, aspirational: SenoRx hopes to expand the market, expects to be a price leader, believes its product will be proven effective, and desires to be used in a broader range of clinical indications. These aspirations are, by definition, speculative and as such cannot outweigh the harm Hologic is actually suffering as a result of SenoRx's infringement.

A. Hologic Is Irreparably Harmed By SenoRx's Ongoing Infringement

The irreparable injury being suffered by Hologic flows from its pioneering of the balloon breast brachytherapy market. For years, Hologic — and only Hologic — invested in convincing the medical community to accept and adopt balloon brachytherapy as a safe and effective treatment of breast cancer. Hologic's investment included product development, clinical research, market development, lobbying for reimbursement, physician training, and so on. Magnuson Decl.[12] ¶ 10.

It is not disputed that SenoRx intends to reap the benefits of Hologic's investment. SenoRx boasts that the Contura and MammoSite have the REDACTED [redacted] Ex. O at 6606. REDACTED Ex. W at 6643, 6662, 663, 6685. Given how similar the products are, it is not surprising that SenoRx obtained FDA clearance for the Contura MLB by relying on MammoSite's 5-year clinical data. Ex. X at SRX-HOL00007337. Moreover, it is also not surprising that SenoRx's avowed marketing strategy is REDACTED SenoRx's efforts to freeride on Hologic's investment by infringing patents, REDACTED and recklessly promoting its product for off-label use, will forever change the market and Hologic's image in that market. The irreparable harm inflicted by SenoRx's ongoing infringement is manifest.

1. Hologic Is Entitled To A Presumption Of Irreparable Harm

[12] Declaration of Glenn Magnuson In Support of Plaintiffs' Motion For Preliminary Injunction ("Magnuson Decl."), filed Feb. 6, 2008 (Dkt. # 25).

Irreparable harm is presumed when a clear showing of patent validity and infringement has been made. *Oakley, Inc. v. Sunglass Hut Int'l*, 316 F.3d 1331, 1345 (Fed. Cir. 2003). SenoRx plainly infringes each and every limitation of claim 36 of the '204 patent and claim 1 of the '142 patent. Its invalidity arguments fail: neither Ashpole nor the '774 patent anticipates (respectively) the asserted claims of the '204 and the '142 patent. Thus, Hologic is entitled to a presumption of irreparable harm from SenoRx's continuing infringement. As discussed below, SenoRx fails to rebut this presumption.[13]

2. SenoRx's Marketing Strategy Is To Poach Hologic's Best Customers

SenoRx does not and cannot dispute that "irreparable harm flows from a competitor's attempts to usurp the pioneering company's market position and goodwill." *800 Adept, Inc. v. Murex Securities, Ltd.*, 2007 WL 1101238, * 6 (M.D. Fla. 2007). And here, despite claims that SenoRx hopes (some day) to grow the market, the record is replete with evidence that SenoRx's marketing strategy for the foreseeable future relies on poaching Hologic's most important customers.

In order to deliver treatment using MammoSite, a radiation facility must make a substantial investment, including purchasing and installing an afterloader, which costs about $500,000, fabricating a lead-shielded room called a "bunker," and obtaining licensure from the Nuclear Regulatory Commission.[14] *Cf.*, Ex. Y (Gearhart) at 17:20-18:1; Ex. Z (Israel) at 52:3-11. Hologic has spent most of the last decade convincing doctors to make this investment and move from whole breast

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[13] SenoRx's arguments notwithstanding, under current Federal Circuit precedent, Hologic is entitled to a presumption that it will be irreparably harmed if SenoRx is not enjoined. *See Abbott Labs. v. Andrx Pharms., Inc.*, 452 F.3d 1331 (Fed. Cir. 2006) (suggesting the continued viability of the presumption of irreparable harm in the preliminary injunction context by stating "Abbott has not established a likelihood of success [and therefore] is no longer entitled to a presumption of irreparable harm."); *cf. Nat'l League of Junior Cotillions, Inc. v. Porter*, No. 3:06-cv-508-RJC, 2007 WL 231823, *5 & n.14 (W.D.N.C. Aug. 9, 2007) (discussing lack of agreement on effects of *eBay* on preliminary injunctive relief). Though the Federal Circuit has not conclusively ruled on the presumption after *eBay, see, e.g.*, *Amando v. Microsoft Corp.*, -- F.3d --, 2008 WL 495760, *4 n.1 (Fed. Cir. Feb. 26, 2008); *Sanofi-Synthelabo v. Apotex, Inc.*, 470 F.3d 1368, 1383 n.9 (Fed. Cir. 2006), this evidentiary presumption is not the same as the presumption of an entitlement to a permanent injunction considered in *E-Bay*. Thus, *eBay* is not controlling; that other district courts may have decided otherwise is of no consequence.

[14] Some of these facilities can, of course, be used for other applications.

irradiation to MammoSite. Current MammoSite facilities stand as a ready-made market for nascent balloon brachytherapy devices such as the Contura.

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SenoRx's assertion that its marketing strategy is irrelevant to the present Motion because there is no evidence that customers tend to remain loyal to suppliers (Opp. at 31) is contradicted by its own corporate designee. Mr. Gearhart testified that REDACTED

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Ex. Y (Gearhart) at 84:4-10. Hologic stands to lose this customer loyalty if SenoRx is allowed to infringe the patents-in-suit pending trial, and Hologic may never be able to convince its former customers to return to MammoSite.

3. Price Erosion Is Likely To Irreparably Harm Hologic

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Despite its protestations that SenoRx has no plans to erode pricing in the balloon market, REDACTED Ex. EE (Magnuson) at 140:22-143:1. REDACTED Magnuson Decl. ¶ 19. More recently, independent market analyst Canaccord Adams reports that the Contura has a below-market average selling price (ASP), is providing early adopters with the device at no charge, and is swapping out inventory of competitor products, including the MammoSite, and/or paying restocking fees. Ex. VV at 2354; Ex. WW at 2360-2361; *See also* Ex. YY at SRX-HOL00003362-67; Ex. XX at SRX-HOL00006892-93 (showing transfer prices of $0.00). Canaccord Adams predicts that these offsets will decline throughout the year, leaving an ultimate ASP in the $2500-$2700 range – well below the current selling price of the MammoSite ($2750) and the current list price of the Contura (also $2750). SenoRx has already embarked on its charted course to erode pricing in the market. REDACTED Ex. II at 7316-7317.

As Ms. Davis, Hologic's expert, explains, the specter of price erosion in this context is not surprising. Before SenoRx began marketing Contura, Hologic was the only significant supplier of balloon brachytherapy products. When a market changed from one major player to two who now compete for the same customers, price erosion will usually occur. Davis Decl. ¶ 22-23.

Indeed, as Mr. Magnuson testified, REDACTED Ex. EE (Magnuson) at 133:15-134:7. REDACTED Thus, price erosion due to SenoRx's presence in the market has already begun to occur. Davis Decl. ¶ 22.

Once the price for MammoSite falls, it would be difficult, if not impossible, for Hologic to recover its previous price point. A lower price means higher profits margins for hospital that use MammoSite. In response to those rising margins, Medicare reimbursement for MammoSite procedures would be lowered. *See* Davis Decl. ¶ 19. Once lowered, these reimbursement rates are almost never raised. *Id.* Thus, following price erosion, Hologic could not raise its prices back to

current levels. The market would be forever changed, and Hologic will have lost its opportunity to fully recoup its massive investment in converting the nascent market.

4. Hologic Is Exposed To A Risk Of Irreparable Loss Of Reputation And Goodwill In The APBI Market

Because SenoRx's Contura product shares the same delivery method and utilizes the same equipment as MammoSite (in contrast to the Xoft electronic brachytherapy product), any failing on the part of Contura may be attributed to the APBI market as whole, and could reflect on the MammoSite product specifically. Magnuson Decl. ¶¶ 22-23; Davis Decl. ¶ 32. This would besmirch the reputation of Hologic's patented technology in the eyes of customers and Hologic would lose a significant but unquantifiable amount of the over $160 million investment it made, including "to educate breast surgeons and radiation oncologists about the MammoSite product, to analyze the clinical data that have been accumulating over the last five years of patient use, and to make further improvements to the MammoSite product." Magnuson Decl. ¶¶ 5-6. The Federal Circuit has held that "[h]arm to reputation resulting from confusion between an inferior accused product and a patentee's superior product is a type of harm that is often not fully compensable by money because the damages caused are speculative and difficult to measure." *Reebok Int'l v. J. Baker, Inc.*, 32 F.3d 1552, 1558 (Fed. Cir. 1994). Hologic's reputation as an innovator and the reputation of MammoSite as a safe and effective treatment could be threatened by the entry of SenoRx's similar yet untested product, causing permanent and unquantifiable – and, therefore, irreparable – harm.

In addition, irreparable harm also accrues from allowing an infringer to continue educating medical practitioners, thereby allowing an infringer to infiltrate the market, to the detriment of Hologic's reputation as a market leader. *Ethicon Endo-Surgery v. United States Surgical Corp.*, 855 F. Supp. 1500, 1516 (S.D. Ohio 1994) (finding persuasive argument that allowing infringers to educate surgeons as they learn a new technique may allow those infringers to dominate the market); *Critikon, Inc. v. Becton Dickinson Vascular Access, Inc.*, 1993 WL 330532, *11 (D. Del. Jul. 16, 1993) (preliminarily enjoining alleged infringer, noting that public interest was best served by minimizing disruption to hospitals selecting catheters, reasoning that if the patentee ultimately prevailed,

"disruption will result in not only the hospitals presently using the [catheter] device, but in addition, all of the hospitals which may be persuaded to begin using it between now and trial.").

5. SenoRx May Well Be Judgment Proof

SenoRx has not demonstrated it has assets sufficient to pay any money judgment likely to be awarded in this matter. Mr. Weinstein declares that "SenoRx has more than adequate assets to fund any damages payment." Weinstein Decl. ¶¶ 30-32. He claims that the company has nearly $28 million in cash, cash equivalents, and short term investments, and total assets valued at $42.1 million. *Id.*; Weinstein Decl.[16] ¶ 19; Davis Decl. ¶ 35. REDACTED [redacted] Ex. FF (Weinstein) 123:21-126:2; Ex. SS at 6; Ex. TT at SRX-HOL00002761. Moreover, REDACTED [redacted]. Ex. RR at 37. Continued losses will also erode the future financial profile of SenoRx and decrease reported asset levels, perhaps to a point where SenoRx would become insolvent and unable to pay damages. Davis Decl. ¶ 36.

6. Hologic's License With Xoft Supports A Finding Of Irreparable Harm

Hologic's license to Xoft, given in settlement of patent infringement litigation, does not show that Hologic is willing to accept money for SenoRx's infringement. It is well-settled law that the existence of a license does not compel denial of injunctive relief. *Abbott Labs. v. Sandoz, Inc.*, 500 F. Supp. 2d 807, 843 (N.D. Ill. 2007) ("[T]he fact that patentees entered into settlement agreements does not diminish the limitations of monetary damages in this case due to the substantial intangible losses that accompany market share and revenue erosion."); *Rosen Entm't Sys., LP v. Eiger Vision*, 343 F. Supp. 2d 908, 919 (C.D. Cal. 2004) (granting preliminary injunction despite license to other former infringers); *see also Sanofi-Synthelabo v. Apotex, Inc.*, 470 F.3d 1368, 1382 (Fed. Cir. 2006) ("[M]erely because a patentee is able to identify a monetary amount that it deems sufficient to avoid or

[16] Declaration of Roy Weinstein In Support Of Defendant's Opp. ("Weinstein Decl.")

end litigation does not necessarily mean that it automatically forgoes its right to seek a preliminary injunction or that any potential irreparable harm ceases to exist if infringement resumes.")

In any event, unlike SenoRx, Xoft does not compete with MammoSite in any sense to the same degree as SenoRx's Contura and so the license to Xoft does not negate the irreparable harm that SenoRx inflicts. Xoft's system is significantly different than the MammoSite – Xoft uses an electronic x-ray source to generate radiation, with a feature set vastly different from those of the Hologic and SenoRx. The chart below summarizes these differences.

Features	MammoSite	SenoRx	Xoft
Radionuclide radiation source	**yes**	**yes**	no
Customer is Radiation oncologist	**yes**	**yes**	no
Requires licensure and oversight from Nuclear Regulatory Commission	**yes**	**yes**	no
Requires radiation-safe bunker	**yes**	**yes**	no
Requires specialized afterloader to store and load radiation sources into the applicator device	**yes**	**yes**	no

See Ex. QQ; Ex. JJ at SRX-HOL00002232; Ex. BB at 7175-7176; Ex. GG at 6583; Ex. Z (Israel) at 50:1-3, 50:7-14-52:11, 54:1-9; 54:20-55:4, 55:18-56:10.

Xoft markets its device to facilities that have not obtained a license from the Nuclear Regulatory Commissions and/or do not have the means or desire to do so. These customers cannot use MammoSite. Similarly, because existing MammoSite customers have already invested heavily to become licensed for radioactive brachytherapy, they likely have no need or desire for Xoft's product. That Xoft remains only a fringe player in the brachytherapy market in which SenoRx and Hologic compete is recognized by practicing brachytherapists. *See, e.g.*, Ex. HH (Arthur) at 54:22-57:19.[17]

[17] "A. If [Xoft] get to the point where they can actually shape direct dose, modulate the energies and so forth, that takes it to a new level that's not available, and we would be interested in getting involved. Q. When you say it's not available, their current system doesn't have the capability? A. That's correct."

REDACTED

7. Hologic Filed Its Motion At The Earliest Reasonable Time

Hologic did not unreasonably delay by bringing the instant Motion only weeks after SenoRx's commercial launch of Contura. Contura sales were no more than REDACTED, and many of those sales were potentially within the FDA research exemption of 35 USC 271(e)(1) and thus not actionable. It was only with the full commercial launch of Contura announced first on January 17, 2008, and the attendant assault on Hologic's customer base, that the need for a preliminary injunction became manifest.

In any event, although courts may consider delay in moving for preliminary relief as one factor in its assessment of irreparable harm, "the majority of infringement cases where preliminary injunctive relief has been denied involved delays of more than one year." *Henkel Corp. v. Coral, Inc.*, 754 F. Supp. 1280, 1322 (N.D. Ill. 1990); *Rosen Entm't Sys., LP v. Eiger Vision*, 343 F. Supp. 2d at 919 (C.D. Cal. 2004) (granting preliminary injunction despite 5 month delay between notifying defendant of alleged infringements and filing suit and pursuing injunctive relief). Courts acknowledge several legitimate reasons to delay moving for preliminary relief, including conducting Rule 11 pre-filing investigations,[18] economic business concerns,[19] and ongoing discovery.[20] Hologic moved expeditiously to prepare its motion papers following SenoRx's commercial launch.

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[18] *Canon Inc. v. GCC Int'l Ltd.*, 450 F. Supp. 243, 256 (S.D.N.Y. 2006)(granting preliminary injunction, noting that 7 months delay for prefiling investigation had not demonstrably prejudiced defendants); *Young v. Lumenis, Inc.*, 301 F. Supp. 2d 765, 772 (S.D. Ohio 2004)(granting preliminary injunctive relief despite 7 month delay for Rule 11 prefiling investigation); *Abbott Labs. v. Sandoz, Inc.*, 500 F. Supp. 2d 807, 843 (N.D. Ill. 2007).

[19] *Du Pont de Nemours v. Polaroid Graphics Imaging,* 10 U.S.P.Q.2d 1579 (D. Del. 1989)(holding that delay until the infringement litigation was economically worthwhile is acceptable).

[20] *Medtronic, Inc. v. Daig Corp., 221 U.S.P.Q. 595 (D. Minn. 1983); Jacobsen v. Cox Paving Co.*, 19 U.S.P.Q. 1641, 1655 (D. Ariz. May 16, 1991).

B. The Balance Of Harms Weighs In Hologic's Favor

Because the balance of harms weighs overwhelmingly against SenoRx, issuance of a preliminary injunction is appropriate. The hardship to SenoRx once enjoined is indistinct from the hardship inflicted on any infringer: SenoRx may well lose an opportunity to burst into a burgeoning market and rapidly acquire market share and assets with an infringing product. Hologic, on the other hand (as discussed within Plaintiffs' Opening Brief and this Reply), absent the protection of an injunction, will suffer a loss of goodwill, reputation, and market share (and consequent revenue and profits), as well as irrecoverable price erosion injury. Moreover, SenoRx's inability to enter the market and begin earning profits earlier does not trump the value that will be lost in Hologic's patent rights absent injunctive relief. *Glaxo Group Ltd. v. Apotex, Inc.*, 64 Fed. App'x 751, 756 (Fed. Cir. 2003). *Oakley, Inc. v. Sunglass Hut Int'l*, No. SA CV 01-1065 AHS, 2001 WL 1683252, at * 11 (C.D. Cal. Dec. 7, 2001), *aff'd* 316 F.3d 1331 (Fed. Cir. 2003). These losses, coupled with the threats to the public interest (discussed below), warrant the issuance of an injunction.

SenoRx's expert, Mr. Weinstein, opines that Hologic cannot be irreparably harmed, and that an injunction should be denied, purely because the magnitude of Hologic's MammoSite sales is, in his view, small compared to Hologic's entire business. Ex. FF (Weinstein) at 112:20-113:6. This rule is contrary to law, because it would mean that disparities in size between the patentee and the accused infringer impact whether a preliminary injunction may be awarded. *See Bell & Howell Document Mgmt. Prods. Co. v. Altek Systems*, 132 F.3d 701, 708 (Fed. Cir. 1997) ("Small parties have no special right to infringe patents simply because they are small.").

C. The Public Interest Would Be Best Served by an Injunction

SenoRx's arguments concerning the public interest are undermined by two indisputable facts: (1) unlike MammoSite, there are no clinical studies, peer-reviewed articles or other, non-anecdotal bases to claim that Contura is effective, and (2) much of Contura's purported superiority is based on an untested used of Contura in a manner ***contrary*** to its FDA-cleared product instructions.

To obtain premarket clearance for the Contura, REDACTED [redacted] Ex. HH (Arthur) at 26:21-27:11. REDACTED [redacted]

REDACTED [redacted] Ex. Y (Gearhart) at 85:8-13, 86:8-11; Ex. Z (Israel) at 82:4-83:2; Ex. HH (Arthur) at 26:21-27:11. REDACTED [redacted] Ex. X at SRX-HOL00007337. REDACTED [redacted] gaining premarket authorization from the FDA on May 23, 2007 to market the Contura. Because it used the same data as the MammoSite, its instruction contain the same indications and warnings as the MammoSite. Ex. W at 6640; Ex. ZZ at SRX-HOL00429-430; Keisch Decl. ¶¶ 9-10.

Neither device is intended for use where the distance between the skin surface and the balloon surface is less than 5mm. Keisch Decl. ¶¶ 9-12. Indeed, the Contura's instructions leave no room for discretion: "***Do not use*** if a skin surface to balloon surface distance of less than 5 mm will result." (Emphasis added..) Ex. JJ at 2232; Ex. KK at 5411. Yet SenoRx is promoting the Contura for use within 5mm of the skin – in fact, it is asserting that this makes Contura better than MammoSite. Keisch Decl. ¶¶ 11-12; Isreal Decl. ¶ 22; Ex. Y (Gearhart) at 134:18-135:18; Ex. W at 6656, 6668-70, 6685. But there is not a shred of clinical data in support of SenoRx's off-label promotion, which is extremely troubling from a public health and safety perspective given that the device is intended to, and does, impact women's health and recovery from cancer. Keisch Decl. ¶¶ 11-12. Most importantly, not one randomized, controlled clinical study demonstrates –or even suggests—that any of SenoRx's touted benefits is anything more than rank speculation. Ex. Y (Gearhart) at 85:8-13, 86:8-11; Ex. HH (Arthur) at 26:21-27:11, 31:20-35:18. As Dr. Israel testified:

> Q There has been no clinical study done of the risks presented by a balloon with a skin bridge less than five millimeters.
> MR. FORKNER: Objection to form.
> A How many have we treated countrywide? Not that many. But so far we have not seen that happen. It's something we will be looking at as we go forward.
> . . .
> Q There could be others [risks] that are unforeseen?
> A "Could be" is -- you know, I guess anything is possible, but I've not heard anything else discussed or -- and I can't think of anything that would be a reasonable issue to put on the table.
> Q And without data, we wouldn't really know at this point; is that right?
> MR. FORKNER: Objection to form.
> A We don't have enough data for any – no.

Ex. Z (Israel) at 126:10-17, 127:4-15. Nor do any peer-reviewed reports assessing the off-label usage of the Contura exist. Ex. Y (Gearhart) at 85:8-13, 86:8-11. SenoRx relies on anecdotes to justify its

decision to market the Contura off-label. Ex. Y (Gearhart) at 55:5-56:8; Ex. Z (Israel) at 64:1-5; Israel Decl. at ¶¶ 21-23. Such uncertainty may well drive the market back towards a greater reliance on the whole breast irradiation treatment. Keisch Decl. ¶ 8; *Cf.,* Ex. HH (Arthur) at 52:10-53:5[21].

Tellingly, after Hologic's filed the Amended Complaint accusing SenoRx of Lanham Act violations for its off-label promotion, REDACTED [redacted], SenoRx violates federal law by promoting the Contura for off-label usage. *Alpo Petfoods, Inc. v. Ralston Purina Co*., 913 F.2d 958 (D.C.Cir. 1990); *Pfizer, Inc. v. Miles, Inc*., 868 F. Supp. 437, 457 (D. Conn. 1994).

More to the point, REDACTED [redacted] According to Dr. Israel, a product that lacks FDA approval is not considered to be safe and effective. Ex. Z (Israel) at 66:5-11[23], 70:5-8[24]. Indeed, SenoRx is currently launching a significant study to attempt to show the safety and effectiveness of its Contura. Ex. Z (Israel) at 114:6-8, 147:8-14; 150:21-151:7, 151:8-12; Ex. HH (Arthur) at 26:21-47:4. SenoRx's effort to conduct this study ***in the future*** emphasizes that

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[21] "…I can treat those patients with standard external beam radiotherapy, possibly multicatheter partial breast brachytherapy, which I did on one case in the sense situation that you're speaking of, or even 3-D conformal if they're on protocol."

[22] REDACTED [redacted]

[23] "What kind of information does, in your view, the medical community require before something is believe to be safe and effective for a particular treatment? A. FDA approval."

[24] Can you tell me what kind of circumstances would lead you to use a product if it wasn't FDA approved? A. I can't."

such data are not extant today – and that the efficacy and toxicity resulting from use of the Contura off-label are untested, and therefore, unknown at the present time.

To support its opposition, SenoRx hired two physicians to extol the virtues of the Contura: Dr. Douglas Arthur and Dr. Phil Israel. Neither is an unbiased witness, as each has been paid by SenoRx to support its device. Ex. Z (Israel) at 41:20-42:2; Ex. HH (Arthur) at 15:10-16:12. Both admit that the Contura does not outperform the MammoSite when used according to the product labeling at a 5 mm or greater balloon-surface-to-skin-surface distance. Ex. Z (Israel) at 107:8-13; Ex. HH (Arthur) at 92:4-2; 95:2-12. Neither doctor can provide any objective, scientific data to support their beliefs that the Contura is superior to the MammoSite – at least for off-label usage. Ex. Z (Israel) at 65:1-5 ("Are you aware of any published data regarding the safety and effectiveness of the Contura MLB? …A. No."); Ex. HH (Arthur) at 19:12-20:2; 26:21-27:11. As such, any opinions expressed by these physicians about the impact of the Contura on the market are purely speculative.

Dated: HOWREY LLP

By: /s/
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